Dendritic and axonal targeting patterns of a genetically-specified class of retinal ganglion cells that participate in image-forming circuits.

Journal: Neural Dev

Publication Year: 2014

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PubMed link: 24495295

Funding Grants: UCSC Shared Stem Cell Facility, UCSC CIRM Training Program in Systems Biology of Stem cells, UCSC Shared Stem Cell Facility

Public Summary:
The retina is the part of the central nervous system that detects light and transduces it into electrical signals that are relayed to the brain via the axons of the retinal ganglion cells (RGCs). There are numerous functional types of RGCs, each participating in circuits that encode a specific aspect of the visual scene. This functional specificity is derived from distinct RGC morphologies and selective synapse formation with other retinal cell types; yet, how these properties are established during development remains unclear. Here we show that the transcription factor Isl2 is expressed in a distinct class of RGCs that project axons to the image-forming part of the brain. We find that Isl2+ RGCs have distinct morphologies and dendritic stratification patterns within the retina and project to selective visual nuclei in the brain. Molecular analysis shows that most alpha-RGCs, indicated by expression of SMI-32, are also Isl2-GFP RGCs. Taken together, these data suggest that Isl2+ RGCs comprise a distinct class and support a role for Isl2 as an important component of a transcription factor code specifying functional visual circuits.

Scientific Abstract:
BACKGROUND: There are numerous functional types of retinal ganglion cells (RGCs), each participating in circuits that encode a specific aspect of the visual scene. This functional specificity is derived from distinct RGC morphologies and selective synapse formation with other retinal cell types; yet, how these properties are established during development remains unclear. Islet2 (Isl2) is a LIM-homeodomain transcription factor expressed in the developing retina, including approximately 40% of all RGCs, and has previously been implicated in the subtype specification of spinal motor neurons. Based on this, we hypothesized that Isl2+ RGCs represent a related subset that share a common function. RESULTS: We morphologically and molecularly characterized Isl2+ RGCs using a transgenic mouse line that expresses GFP in the cell bodies, dendrites and axons of Isl2+ cells (Isl2-GFP). Isl2-GFP RGCs have distinct morphologies and dendritic stratification patterns within the inner plexiform layer and project to selective visual nuclei. Targeted filling of individual cells reveals that the majority of Isl2-GFP RGCs have dendrites that are monostratified in layer S3 of the IPL, suggesting they are not ON-OFF direction-selective ganglion cells. Molecular analysis shows that most alpha-RGCs, indicated by expression of SMI-32, are also Isl2-GFP RGCs. Isl2-GFP RGCs project to most retino-recipient nuclei during early development, but specifically innervate the dorsal lateral geniculate nucleus and superior colliculus (SC) at eye opening. Finally, we show that the segregation of Isl2+ and Isl2- RGC axons in the SC leads to the segregation of functional RGC types. CONCLUSIONS: Taken together, these data suggest that Isl2+ RGCs comprise a distinct class and support a role for Isl2 as an important component of a transcription factor code specifying functional visual circuits. Furthermore, this study describes a novel genetically-labeled mouse line that will be a valuable resource in future investigations of the molecular mechanisms of visual circuit formation.